60. (Twice Amended) A method for downregulating CCR5 expression in a T cell, comprising contacting the T cell with a solid phase surface comprising an anti-CD28 antibody and an anti-CD3 antibody *in vivo*, thereby downregulating CCR5 expression in a T cell, wherein the T cell is more resistant to infection by an M-tropic HIV isolate than a T cell not contacted with the solid surface.

F1

75. (Twice Amended) A method for downregulating HIV-1 fusion cofactor expression in a T cell, comprising contacting the T cell with a solid phase surface comprising an anti-CD28 antibody and an anti-CD3 antibody *in vivo*, thereby downregulating HIV-1 fusion cofactor expression in the T cell, wherein the T cell is more resistant to infection by an M-tropic HIV isolate than a T cell not contacted with the solid surface.

F2

REMARKS

Claims 1, 55, 60, 75, and 87-94 stand pending in the Application.

Claims 60 and 75 have been amended to require that the T cell is more resistant to infection by an M-tropic HIV isolate than a T cell not contacted with the solid surface. These amendments contain no new matter, as support for these amendments can be found throughout the Application, for example, at page 34, line 32 through page 37, line 28. Pursuant to the provisions of 37 C.F.R. §1.121(c)(1)(ii), a marked-up version of the amended claims is provided herewith as Appendix A. In addition, pursuant to the provisions of 37 C.F.R. §1.121(c)(3), a copy of the claims pending following the entry of this Amendment is provided as Appendix B.

Former Rejections

Applicants acknowledge the withdrawal of the former rejection of claim 91 under 35 U.S.C. § 112, first paragraph (Advisory Action mailed April 25, 2002).

Rejection under 35 U.S.C. §102(a)

Claims 1, 55, 87-90, 92, and 94 stand rejected under 35 U.S.C. § 102 (a) for allegedly being anticipated by Levine *et al*, Science 272: 1939-1943 (June 1996).

To overcome this ground for rejection, Applicants submit herewith a second *In re Katz* Declaration by Dr. Carl H. June, one of the co-inventors of the instant application. The Declaration states that the work described in the Levine *et al.* paper is Applicants' own work. The Levine *et al.* paper was published within one year of the filing date of the parent application of this Application. As such, the reference cannot be properly used as prior art against the Applicants under 35 U.S.C. § 102(a). Accordingly, Applicants respectfully request withdrawal of this rejection.

Note that in preparing the *In re Katz* Declaration enclosed herewith, Applicants discovered that Bruce L. Levine, who should have been named as an inventor on the Application, was inadvertently not named. The *In re Katz* Declaration enclosed herewith reflects that Dr. Levine is indeed an inventor of the Application. We will shortly be filing a Petition to Correct the Inventorship for this Application, to correctly name all five inventors.

Rejection under 35 U.S.C. §102(e)

Claims 1, 55, 60, 75 and 87-89, 92, and 94 stand rejected under 35 U.S.C. §102(e) as being purportedly anticipated by Chang, U.S. Patent No. 6,129,916. Applicants respectfully traverse this rejection.

As this rejection applies to independent claims 1 and 55, and the claims dependent thereon, Applicants respectfully aver that Chang does not teach, explicitly or inherently, contacting T cells with a solid phase surface comprising anti-CD28 and anti-CD3 antibodies *in vitro*. Rather, Chang focuses on methods for increasing activation without causing immunosuppression by administering his immunoregulatory conjugates *in vivo*. Indeed, the only time Chang describes activation of T cells *in vitro* is to provide the rationale for his *in vivo* method (see, *e.g.*, Chang, col. 11, lines 26-29).

Because Chang does not teach a required limitation of claims 1 and 55 (and claims dependent thereon), Chang does not anticipate these claims. Accordingly, Applicants respectfully request that this ground for rejection be reconsidered and withdrawn.

As this ground for rejection applies to independent claims 60 and 75 (and the claims dependent thereon), Applicants respectfully aver that the claims, as presently amended, are not anticipated by Chang. Nowhere in Chang is there mention that a T cell, upon contact with a solid phase surface comprising anti-CD28 and anti-CD3 antibodies, becomes more resistant to infection by an M-tropic HIV isolate, as is now required by the claims. Because Chang does not teach a required limitation of claims 60 and 75 (and claims dependent thereon), Chang cannot anticipate these claims. Accordingly, Applicants respectfully request that this ground for rejection be reconsidered and withdrawn.

Rejection under 35 U.S.C. §103(a)

Claims 1, 55, 60, 75, 91, and 93 stand rejected under 35 U.S.C. § 103 (a) as purportedly being obvious over the combination of either Levine *et al.* or Chang in view of Shattil, U.S. Patent No. 5,561,047. Applicants respectfully traverse this rejection.

a) Levine et al. in view of Shattil

As discussed above, Levine *et al.* is not a prior art reference against Applicants' claims. In light of this argument and the concurrently submitted *In re Katz* Declaration, the rejection of the claims over Levine *et al.* and Shattil is overcome.

a) Chang in view of Shattil

As this ground for rejection applies to independent claims 1 and 55, and the claims dependent thereon, as discussed above, Applicants respectfully aver that Chang does not teach or suggest contacting T cells with a solid phase surface comprising anti-CD28 and anti-CD3 antibodies *in vitro*. Rather, Chang actually teaches away from in vitro methods, stating, "many of these *in vivo* effects would not be predicted from the

known *in vitro* effects or the *in vivo* effects with the whole antibodies" (Chang, col. 11, line 13-15).

Nor does Shattil cure the deficiencies of Chang. Shattil nowhere teaches or suggests contacting T cells with a solid phase surface comprising anti-CD28 and anti-CD3 antibodies *in vitro*. Since both Chang and Shattil fail to teach or suggest a required limitation of the claims, their combination cannot render the claimed invention obvious to the ordinarily skilled artisan. Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

As this ground for rejection applies to independent claims 60 and 75, and the claims dependent thereon, as discussed above, Chang nowhere teaches or suggests that a T cell, upon contact with a solid phase surface comprising anti-CD28 and anti-CD3 antibodies, becomes more resistant to infection by an M-tropic HIV isolate, as is required by the present claims. Nor does Shattil teach or suggest this claim limitation. Because neither Chang nor Shattil teaches or suggests a required limitation of claims 60 and 75 (and claims dependent thereon), their combination cannot render these claims obvious Accordingly, Applicants respectfully request that this ground for rejection be reconsidered and withdrawn.

CONCLUSION

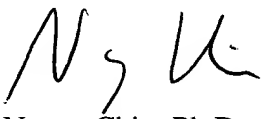
Applicants believe that all of the outstanding rejections of record have been overcome by amendment and/or argument. Accordingly, the claims are now believed to be in condition for allowance. Applicants respectfully request that the Examiner issue a timely Notice of Allowance.

Accompanying this Amendment is a Request for Continued Prosecution, as well as a Petition for a Five Month Extension of Time for responding to the Notice of Appeal filed April 9, 2002. As November 9, 2002 fell on a Saturday (and since Monday, November 11, 2002 was a Federal Holiday), this submission is timely. Please charge the fees outlined on the attached Fee Transmittal to our Deposit Account No. 08-0219.

No additional fees are believed to be due in connection with this correspondence. However, please charge any payments due or credit any overpayments to our Deposit Account No. 08-0219.

The Examiner is invited to telephone the undersigned at the telephone number given below in order to expedite the prosecution of the instant application.

Respectfully submitted,
HALE AND DORR LLP



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Dated: November 12, 2002

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APPENDIX A

Marked-up Version of the Amended Claims Pursuant to 37 C.F.R. §1.121(c)(1)(ii)

60. (Twice Amended) A method for downregulating CCR5 expression in a T cell, comprising contacting the T cell with a solid phase surface comprising an anti-CD28 antibody and an anti-CD3 antibody *in vivo*, thereby downregulating CCR5 expression in a T cell, wherein the T cell is more resistant to infection by an M-tropic HIV isolate than a T cell not contacted with the solid surface.

75. (Twice Amended) A method for downregulating HIV-1 fusion cofactor expression in a T cell, comprising contacting the T cell with a solid phase surface comprising an anti-CD28 antibody and an anti-CD3 antibody *in vivo*, thereby downregulating HIV-1 fusion cofactor expression in the T cell, wherein the T cell is more resistant to infection by an M-tropic HIV isolate than a T cell not contacted with the solid surface.

APPENDIX B

Claims Following Entry of this Amendment

1. A method for downregulating HIV-1 fusion cofactor expression in a T cell, comprising contacting the T cell with a solid phase surface comprising an anti-CD28 antibody and an anti-CD3 antibody *in vitro*, thereby downregulating HIV-1 fusion cofactor expression in the T cell.

55. A method for downregulating CCR5 expression in a T cell, comprising contacting the T cell with a solid phase surface comprising an anti-CD28 antibody and an anti-CD3 antibody *in vitro*, thereby downregulating CCR5 expression in the T cell.

60. (Twice Amended) A method for downregulating CCR5 expression in a T cell, comprising contacting the T cell with a solid phase surface comprising an anti-CD28 antibody and an anti-CD3 antibody *in vivo*, thereby downregulating CCR5 expression in a T cell, wherein the T cell is more resistant to infection by an M-tropic HIV isolate than a T cell not contacted with the solid surface.

75. (Twice Amended) A method for downregulating HIV-1 fusion cofactor expression in a T cell, comprising contacting the T cell with a solid phase surface comprising an anti-CD28 antibody and an anti-CD3 antibody *in vivo*, thereby downregulating HIV-1 fusion cofactor expression in the T cell, wherein the T cell is more resistant to infection by an M-tropic HIV isolate than a T cell not contacted with the solid surface.

87. The method of any one of claims 1, 55, 60, or 75, wherein the anti-CD3 antibody is an anti-human CD3 monoclonal antibody.

88. The method of any one of claims 1, 55, 60, or 75, wherein the anti-CD28 antibody is an anti-human CD28 monoclonal antibody.

89. The method of any one of claims 1, 55, 60, or 75, wherein said solid phase surface is a bead.

90. The method of claim 89, wherein the bead is a magnetic immunobead.

91. The method of any one of claims 1 or 55, wherein said solid phase surface is a tissue culture dish.

92. The method of any one of claims 1, 55, 60, or 75, wherein the anti-CD3 antibody and the anti-CD28 antibody are immobilized on the solid phase via a covalent modification.

93. The method of any one of claims 1, 55, 60, or 75, wherein the anti-CD3 antibody and the anti-CD28 antibody are immobilized on the solid phase surface via an avidin-biotin complex.

94. The method of any one of claims 1, 55, 60, or 75, wherein the anti-CD3 antibody and the anti-CD28 antibody are directly immobilized on the solid phase surface.